Burden of Hodgkin and non-Hodgkin lymphoma in Spain over a 10-year period: Productivity losses due to premature mortality

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ABSTRACT

Background: Cancer is annually responsible for millions of deaths in Europe and billions of euros in productivity losses; the estimated mortality rate of lymphoma was of 7.07 per 100,000 individuals in Spain in 2018. This study aimed to evaluate the burden that lymphoma mortality represents for the Spanish society.

Methods: The human capital approach was used to estimate the costs derived from premature mortality due to lymphoma between 2008 and 2017.

Results: The number of deaths attributable to lymphoma increased steadily over the study period; the major number of deaths occurred among males aged 80 to 84 years. During the study period, 97,069 years of productive life were lost, a parameter that decreased noticeably over time due to the reduction in the number of deaths at working age. Productivity losses decreased accordingly. Lymphoma represented the 45.36% of losses due to hematological malignancies, generating €121 million in losses the year 2017. Hodgkin lymphoma was, among hematological malignancies, the malignancy accounting for the highest portion of losses per individual.

Conclusions: Lymphoma represents a significant burden that can be reduced with the implementation of improved diagnosis and treatment methods, which must be taken into account in resource allocation and management policies.

Keywords

Hodgkin lymphoma; Non-Hodgkin lymphoma; Years of Productive Life Lost; Disease burden; Spain.

1. Introduction

Lymphomas comprise a diverse group of hematological malignancies with broadly varying clinical features, histology, phenotypes, and genetic abnormalities. Generally, lymphomas can be classified as Hodgkin lymphomas (HL) and non-Hodgkin lymphomas (NHL), with NHL further classified into more specific entities according to the cell type that is affected [1]. HL incidence rate peaks in young adults, aged between 20 and 24 years, whereas the incidence of NHL peaks in older adults aged 80 to 89 years [2]. Estimations situate lymphoma age-standardized ten-year survival rate at around 80% for HL and 63% for NHL in European countries, a rate that has steadily increased in both cases during the past 60 years [2]. Still, the year 2018, lymphoma was responsible for 3.64 deaths per 100,000 individuals worldwide, and represented the 2.88% of deaths due to malignant neoplasms [3].

Cancer is the second leading cause of death worldwide, and the global burden of cancer associated with morbidity and mortality follows an increasing tendency [4]. In Europe, 1.93 million people were estimated to die from cancer in 2018, and it accounted for 50,168,779 disability-adjusted live years (DALYs) and 48,784,557 years of life were lost in 2016 [5,6]. Equally, losses attributed to lost productivity in Europe were estimated to reach the €126 billion in 2009, around €2.5 billion only in Spain [7,8]. Malignant neoplasms were responsible for approximately 27% of all deaths in 2018 in the country, and the estimated mortality rate of lymphoma was of 7.07 per 100,000 individuals [3,9]. This major mortality rate is likely to correlate with a significant burden that cancer and lymphoma represent for the Spanish society.

This burden can be reduced through early detection and the use of efficient disease management protocols. Thus, it is essential to gather information on the disease at the population level, and also to conduct economic evaluations that guide healthcare policies.

In this direction, the estimation of productivity losses provides useful data, obtained in its majority via the human capital approach. This method estimates the income and productivity of an individual that are prevented when a premature death occurs [10]. Other methods to estimate lost productivity are the friction cost approach, centered on the losses that take place during the time needed to replace a worker, and the willingness to pay approach that values immaterial costs including pain and distress [11,12].In this context, the aim of this study was to evaluate the burden that Hodgkin and non-Hodgkin lymphoma represent for the Spanish society and to revise mortality in the country over a ten-year period.

2. Patients and methods

Costs derived from premature mortality were measured via the human capital approach, considering the cost from the worker's perspective. Mortality statistics and reference salaries were extracted from the Spanish National Statistics Institute (INE) [13,14], and the study period was set to ten years (2008-2017) to include the most recent available data. Death causes are codified with ICD-10 Cause-of-Death codes within the INE database; all deaths attributed to lymphoma were selected using the codes C81 to C88 and those attributed to other hematological malignancies were selected with the codes C90 to C96.Crude years of productive life lost (YPLLs) due to lymphoma and other hematological malignancies were estimated by multiplying the number of deaths for a given age group by

the expected productive years remaining for each group, fixing retirement age at 65 years. For the calculation of productivity losses, YPLL were corrected using age- and sex-specific annual wages and employment rates [15]. An annual discount rate of 3% was applied to future income values and a sensitivity analysis was conducted considering two alternative discount rates (0% and 6%).

The year 2017 was used as a reference to estimate productivity losses, updating nominal values using the Spanish GDP deflator as considered by the Spanish Central Bank [16].

3. Results

Between the years 2008 and 2017, 2,403 deaths were registered in Spain attributable to Hodgkin lymphoma, whereas non-Hodgkin lymphoma caused 26,660 deaths in the same time period. Males represented, on average, the 57.08% of the deceased per HL, and 54.55% of those per NHL (Table 1). The annual number of deaths attributable to lymphoma grew steadily, increasing from 2,673 in 2008 to 3,090 in 2017, with minor shifts that appeared when examining both disease groups separately.

Overall, the age range with the major number of deaths was 80 to 84 for males and females with HL and females with NHL, conversely, in males with NHL age distribution peaked between 75 and 79 years (Figure 1).

Interestingly, the demographic analysis per age groups revealed a decreasing tendency in the percentage of deaths corresponding to individuals at working age over time (Figure 2A). Such decrease was validated by the clear reduction of crude YPLL over time (Figure 2B), which summed 97,069 over the whole study period.

Productivity losses due to premature mortality were calculated using the year 2017 as a reference. Subsequently, annual losses were projected to retirement age, obtaining a baseline and the results from the sensitivity analysis (Table 2). HL generated €255 million in productivity losses in a ten year period, while NHL reached the €1107 million. The year 2017 losses attributable to lymphoma summed €121 million. A clear decreasing tendency was observed in both cases in line with the values of YPLL, and the losses of HL were reduced almost to the half over the study period.

An evaluation of the weight of the totality of hematological malignancies in the Spanish society was considered of interest in the context of this study. The year 2017, 8,501 individuals died due to hematological malignancies in Spain. Forty percent of the deaths were attributable to leukemia, NHL represented the 33.53%, myeloma the 22.15%, HL the 2.82% and the 0.87% were caused by other malignancies affecting the lymphoid tissue or hematopoietic organs (Figure 3A). The losses originated by hematological malignancies were as well calculated. Total productivity losses reached the €267 million the year 2017, distributed in proportion to the deceased number per cancer type (Figure 3B). Yet, lymphoma was responsible for the 45.36% of all losses due to hematological malignancies, and the losses generated by HL represented a percentage higher than its total number of deaths, suggesting an increased portion of individuals deceased at working age. In accordance, HL accounted for the highest amount of losses per person.

4. Discussion

Cancer caused over 9.5 million deaths globally in 2018 and it has been for several years the second leading cause of death behind cardiovascular diseases [4]. In global classifications,

lung cancer was responsible for the most number of deaths, while lymphoma occupied the 11th position after leukemia; NHL was the eight cancer type in number of deaths in the United States in 2019 [4,17]. The incidence of lymphomas is variable among world regions, with trends either stable or decreasing in most countries, including Spain [18]. The Spanish Ministry of Health estimates that 3,605 individuals were admitted in secondary care centers in 2017 with HL, 18,023 with NHL [19].

Improved management and novel treatments and diagnosis methods have increased early detection and a more efficient treatment of most cancer types, including lymphoma [20,21]. This study portrays a situation in the country that is comparable to that measured in global statistics. The total number of deaths attributable to lymphoma has increased noticeably over the past ten years, although overall survival has improved in the country [22,23]. On the other hand, the portion of individuals deceased after retirement age has increased, indicating that the age of death is augmenting over the years, as survival rates in individuals with an infantile or adolescent onset have improved and appear currently stable in Spain [24].

Consequently, YPLL decreased over the ten years of study for both HL and NHL, with measures of 1,322 and 6,806 per each group in 2017. In spite of this tendency, mortality has been appointed as the main responsible for lymphoma's indirect costs, and such expenses are estimated to surpass those derived from hospital care [25]. Herein, lymphoma generated €121 million in losses the year 2017, a cost that should be taken into consideration in terms of disease management. A previous study developed in Spain estimated the burden of blood cancers in transplanted patients in two Spanish provinces,

reaching the €34 million in 2009 [26]. Although data cannot be extrapolated to the whole country, lymphoma accounted the highest portion of losses per death at the regional level, similarly to the findings of the present study. Similar conclusions have been reached in other countries as the United States, where HL was the second most costly cancer per death [27]. In Spain, comparisons to other cancer types are limited; the year 2017, lung cancer represented a total cost of €1.2 billion, while breast cancer summed €222 million in productivity losses in women as measured in 2014 [28,29]. Hence, an improved management of lymphoma will be of utmost importance for the Spanish society and should be taken into account in healthcare resource allocation.

It is plausible that a number of limitations might have influenced the results obtained. This study evaluates lost productivity costs associated with lymphoma mortality; however, further analyses will be required to evaluate the total burden of lymphoma, taking into account disease morbidity and lost productivity from the time of diagnosis. Hence, the methodology applied herein may result in an underestimation of the disease burden.

5. Conclusions

Lymphoma was responsible for 29,063 deaths in Spain between 2008 and 2017, summing 97,069 YPLLs over the ten-year period. Productivity losses displayed a decreasing tendency due to the increasing age of death; still, Hodgkin lymphoma was of all blood cancers the malignancy accounting for the highest portion of losses per individual. This data underlines the weight of lymphoma within the Spanish population, highlighting the importance of improved management, evaluation of risk factors and early detection programs that possibly yield substantial reductions in mortality and productivity loss.

6. Declarations

6.1 Ethics approval and consent to participate

Ethics committee approval and consent were not required for this study.

6.2 Data availability

The data that support the findings of this study are fully available from the Spanish national statistics institute at http://www.ine.es.

6.3 Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

6.4 Competing interests

The authors report no conflicts of interest.

6.5 Acknowledgements

Not applicable.

7. References

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8. Figures

Figure 1 (A) Total number of deaths due to Hodgkin and (B) non-Hodgkin lymphoma stratified by age (2008-2017).

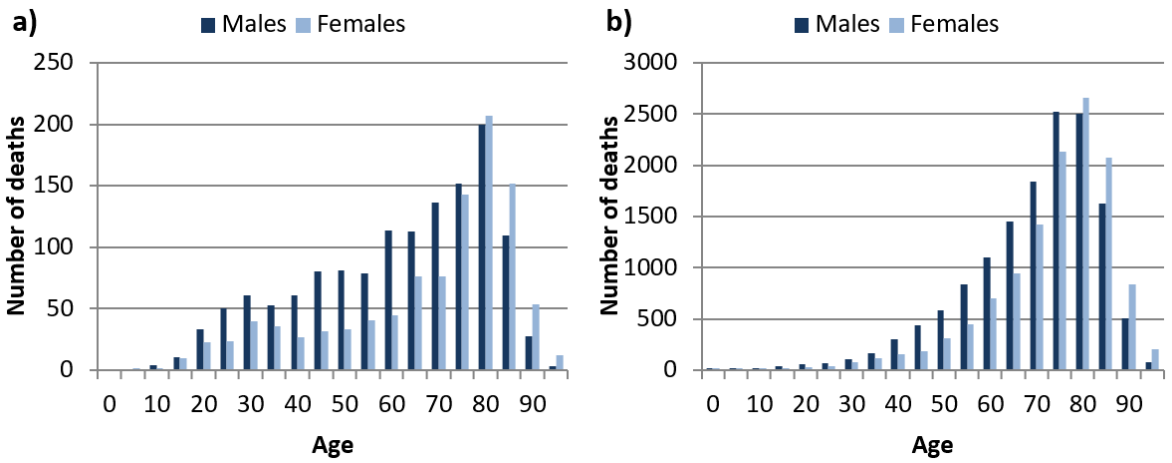
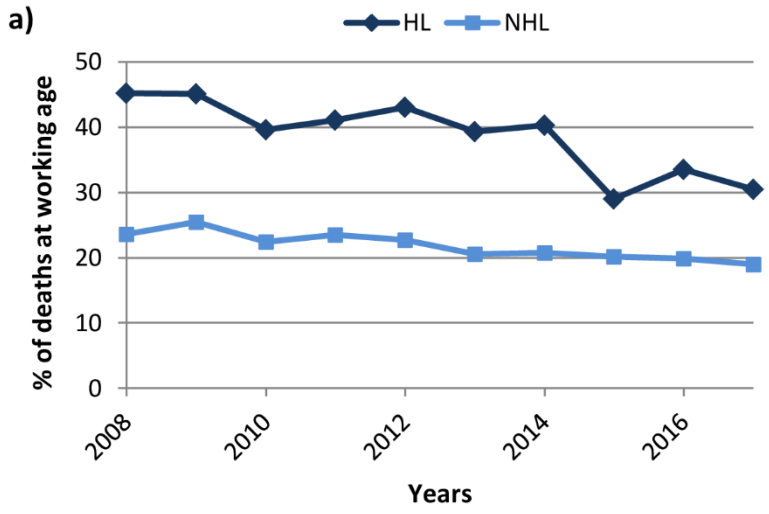


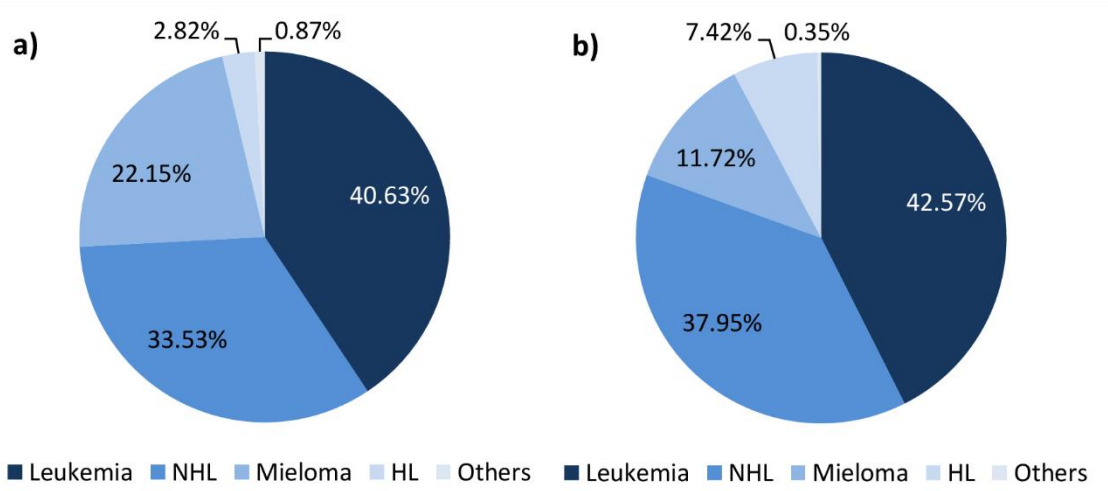
Figure 2 (A) Percentage of deaths at working age over time and (B) years of productive life lost (YPLL) over time (2008-2017).



b)

	YPLL	
	HL	NHL
2008	2,330	8,550
2009	2,514	9,578
2010	2,506	7,291
2011	2,521	8,204
2012	2,148	8,440
2013	1,759	7,274
2014	1,733	7,782
2015	1,282	7,093
2016	1,273	6,663
2017	1,322	6,806

Figure 3 (A) Percentage of deaths and (B) productivity losses caused by hematological malignancies in 2017.



9. Tables

Table 1 Number of deaths attributable to Hodgkin and non-Hodgkin lymphoma in Spain between 2008 and 2017.

Year	Number of deaths			
	Hodgkin lymphoma		Non-Hodgkin lymphoma	
	Males	*Females*	*Males*	*Females*
2008	144	97	1,331	1,101
2009	145	117	1,310	1,205
2010	147	131	1,408	1,136
2011	147	111	1,399	1,207
2012	142	102	1,409	1,302
2013	129	95	1,490	1,264
2014	128	98	1,430	1,293
2015	122	99	1,513	1,254
2016	126	83	1,504	1,254
2017	139	101	1,478	1,372

Table 2 Productivity losses (in million €) due to lymphoma in Spain (sensitivity models 0%; 6%).

Year	Hodgkin lymphoma			Non-Hodgkin lymphoma		
	Baseline	**0%**	**6%**	**Baseline**	**0%**	**6%**
2008	34	35	33	131	135	128
2009	35	36	34	132	136	129
2010	29	30	29	103	106	100
2011	28	29	28	117	120	114
2012	28	29	28	116	119	113
2013	24	24	23	101	104	98
2014	20	21	20	103	106	100
2015	16	17	16	105	108	102
2016	19	20	19	99	101	96
2017	20	20	19	101	104	99
Total	255	262	248	1,107	1,137	1,079